INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

STABILITY TESTING OF DRUG SUBSTANCES AND DRUG PRODUCTS

Q1

Draft version

Endorsed on 11 April 2025

Currently under public consultation

ICH HARMONISED GUIDELINE

STABILITY TESTING OF DRUG SUBSTANCES AND DRUG PRODUCTS

Q1

ICH CONSENSUS GUIDELINE

Stability studies during a product life-cycle

Development

- Stress testing Q1A
- Photostability Q1B
- **Intermediates**
- **Freeze-thaw**
- **Packaging compatibility**
- **Formulation**
- **Clinical trials**
- **Transport (incl. vibration, radiation)**
- **In use**

Submission

- Formal studies Q1A, Q1D, Q1E, Q1F, Q5C
  - *Accelerated*
  - *Long term*
- New dosage forms Q1C
- Commitment batches Q1A, Q1D, Q1E, Q1F, Q5C

Post-approval

- **Follow-up**
- **Changes**

NOT described in the ICH /
described in ICH guidelines

1.2 Scope of the Guideline

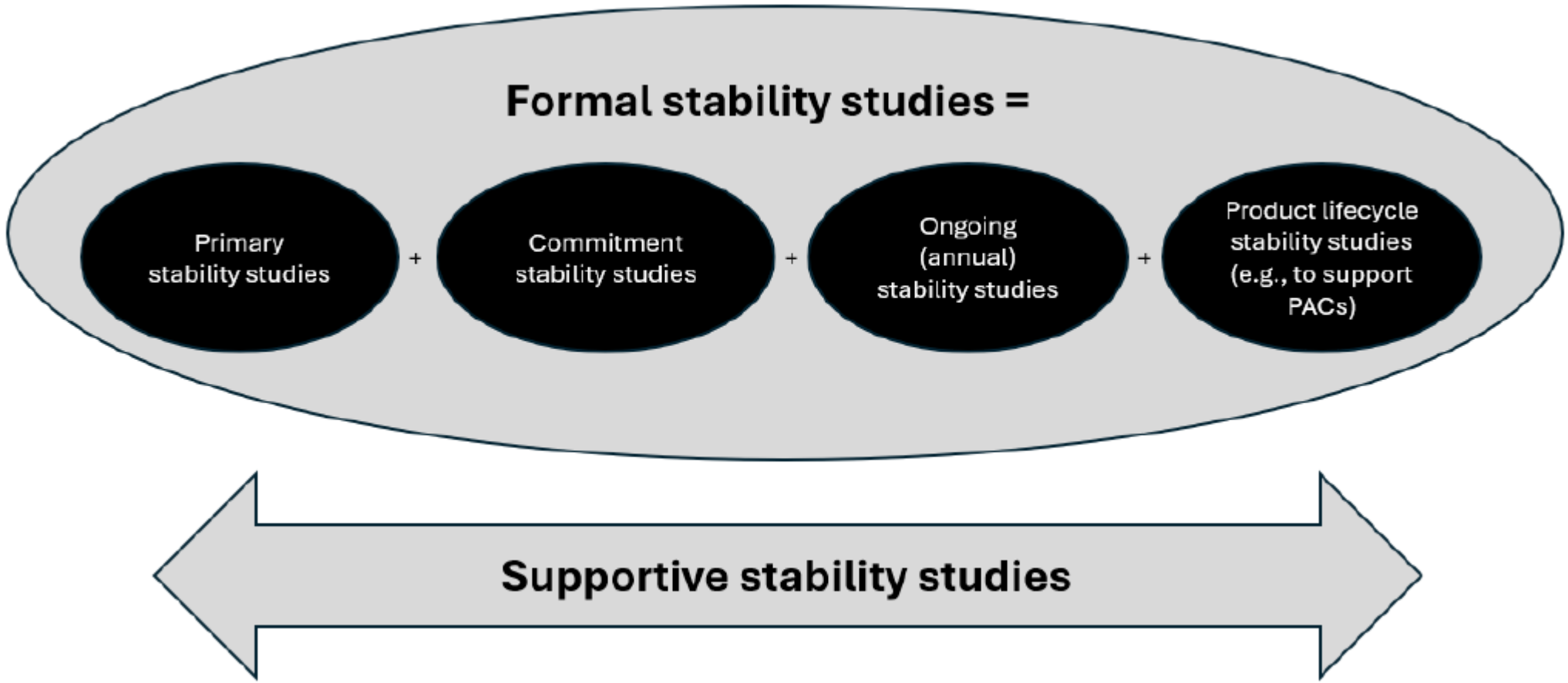
This guideline applies to synthetic and biological drug substances and drug products, including the following:

- Chemically synthesised drug substances including oligonucleotides, polysaccharides and polypeptides (collectively referred to as 'synthetic chemical entities' or 'synthetics' in this guideline), semi-synthetic drug substances and fermentation-derived drug substances.
- Therapeutic proteins/polypeptides, polysaccharides and proteoglycans produced using recombinant DNA (rDNA) technology or isolated from human, animal or plant tissues, other natural sources, including body fluids (such as plasma-derived products), or cell cultures.
- Conjugated products that are made up of proteins/polypeptides linked to another moiety (e.g., antibody-drug conjugate).
- Vaccines, allergenic products, and adjuvants.
- Autologous and allogenic cell-based substances, including those which may be genetically modified *ex-vivo* (refer to Annex 3 – Stability of Advanced Therapy Medicinal Products (ATMPs)).
- Gene therapy products that mediate their effect by the expression (transcription or translation) of transferred genetic materials and genome editing products used to modify cells (refer to Annex 3 – Stability of Advanced Therapy Medicinal Products (ATMPs)).
- The drug constituent part of a combination of a drug product with a medical device (both integral or co-packaged).
- Co-packaged solvents/diluents.
- Natural health products that are regulated as drug products.

Although this guideline is not directly applicable to drug substances and drug products during clinical development stages, the concepts can apply proportionate to increasing level of product and process understanding during pharmaceutical development. The data from development batches that meet primary stability requirements may be used to support a regulatory submission and for product lifecycle management. Refer to Section 15 - Stability Considerations for Commitments and Product Lifecyle Management.

A standard approach to assess each stability-related topic is provided by describing the general principles and strategies to assess stability. In addition, the principles of Quality by Design described within ICH Q8-Q11 and Q14, through enhanced understanding of critical quality attributes (CQAs) and the impact that the manufacturing process can have on these attributes, are applicable to the design of an overall stability strategy.

This guideline addresses all four climatic zones. The principle has been established that if the stability information is generated under a more severe climatic zone storage condition, it would be acceptable in the other climatic zones, provided the information is consistent with this guideline and the labelling and storage statements are in accordance with regional requirements.


Formal stability studies =
Primary stability studies
+
Commitment stability studies
+
Ongoing (annual) stability studies
+
Product lifecycle stability studies (e.g., to support PACs)
Supportive stability studies

2 DEVELOPMENT STABILITY STUDIES UNDER STRESS AND FORCED CONDITIONS

In the context of generating product knowledge, studies may be performed under accelerated and/or stress conditions, including forced conditions. The nature of this testing should be proportionate to the knowledge available, the type of the drug substance or drug product being evaluated and the quality attribute(s) being investigated.

Development studies undertaken to assess the effect of stress on the drug substance and/or drug product can be divided into two categories:

1) Studies conducted under *stress conditions*: Conditions are more severe than the accelerated conditions but not necessarily intended to deliberately degrade the sample.

2) Studies conducted under *forced degradation conditions*: Conditions are intended to deliberately degrade the sample (such as elevated temperature, humidity, pH, oxidation, agitation and light).

2 DEVELOPMENT STABILITY STUDIES UNDER STRESS AND FORCED CONDITIONS

2.1 Development Studies Under Stress Conditions

Stress condition studies can include temperature and humidity levels above accelerated conditions, thermal cycling and freeze-thaw studies, as appropriate. For synthetic chemicals entities, these studies may be conducted on one batch of the drug product and where relevant one batch of the drug substance directly exposed or in a container closure system, as applicable. For biologicals, at a minimum, stress studies may be performed on a single batch of drug product, however, it may be possible to justify using a single batch of drug substance if it is representative of the drug product.

2 DEVELOPMENT STABILITY STUDIES UNDER STRESS AND FORCED CONDITIONS

2.2 Development Studies Under Forced Degradation Conditions

Forced degradation studies may be utilised to investigate potential degradation pathways; gain product knowledge; understand the intrinsic stability of product and used to develop and confirm stability-indicating nature of the analytical procedure (refer to ICH Q2 and ICH Q14). It is acceptable to leverage product knowledge when data is available on identified degradation products and pathways, including scientific literature.

It is recommended to assess forced conditions on a single batch of the drug substance. It should include the effect of elevated temperatures, humidity (e.g., 75% Relative Humidity (RH) or greater) where appropriate, oxidation and photodegradation on the drug substance. Testing should evaluate the susceptibility of the drug substance to hydrolysis across a range of pH values. Also, a combination of forced conditions may be appropriate to test under certain circumstances (e.g., agitation and heat).

2 DEVELOPMENT STABILITY STUDIES UNDER STRESS AND FORCED CONDITIONS

2.2 Development Studies Under Forced Degradation Conditions

For drug products, testing under forced conditions is recommended on a single batch of exposed drug product. It should include the effect of temperature, humidity (e.g., 75% RH or greater) where appropriate and light. Additional forced conditions for specific types of products and dosage forms may be appropriate.

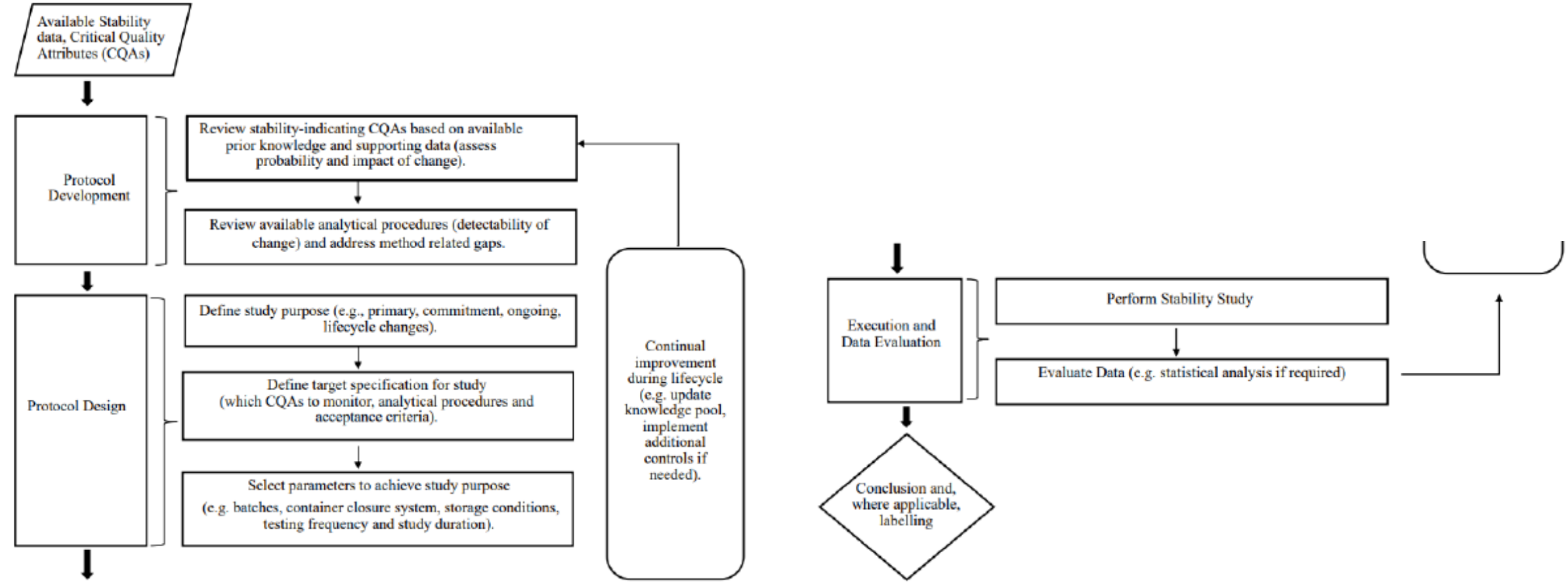
For biologicals, studies under forced degradation conditions should be performed on a single batch of drug substance; alternatively, it may be possible to justify using a single batch of drug product.

3 PROTOCOL DESIGN FOR FORMAL STABILITY STUDIES

A summary of the stability protocol should be provided in a regulatory submission when a re-test period or shelf life is to be established or confirmed.

ICH Q1 STABILITY STUDIES FOR DRUG SUBSTANCES AND DRUG PRODUCTS

Figure 2: General Process Flow for the Development, Design and Execution of a Stability Protocol



3 PROTOCOL DESIGN FOR FORMAL STABILITY STUDIES

Additional protocol considerations for photostability, excursions, short-term storage and in-use conditions are described in the respective sections (refer to Section 8 – Photostability, Section 14.1 – Excursions Outside of a Labelling Claim, Section 10 - Short-Term Storage Conditions and Section 11 – In-Use Stability).

A full design stability protocol is a protocol where at least three batches of the drug substance or at least three batches of each strength of the drug product covering the proposed container closure systems for every combination of all design factors are included and tested at all time points. Alternative approaches to stability protocol design, such as bracketing, matrixing, knowledge- and risk-based protocol reductions and stability models are described in Annex 1 – Reduced Stability Protocol Design and Annex 2 – Stability Modelling. Additional considerations for ATMPs are provided in Annex 3 – Stability of Advanced Therapy Medicinal Products (ATMPs).

Data from the accelerated storage conditions and, if appropriate, from the intermediate storage conditions can be used to evaluate the effect of short-term excursions outside the labelled storage conditions (e.g., during shipping).

3 PROTOCOL DESIGN FOR FORMAL STABILITY STUDIES

3.3 Stability-Indicating Critical Quality Attributes

CQAs should be identified using the principles outlined in ICH Q6A, Q6B and ICH Q8-Q11. When designing a stability protocol in support of a drug substance or drug product, information on the CQAs and their target acceptance criteria should already be available. Based on prior knowledge and development data, the applicant should identify the stability-indicating CQAs, which are those attributes that may change upon storage and may impact the functionality and/or quality of the drug substance or drug product.

Where excipient levels or their properties may change on stability, potentially impacting drug product CQAs, they should be evaluated as part of drug product stability testing, (e.g., levels of surfactant, preservative content). In cases where stabilisers are needed for a biological drug substance, the same considerations should be applied. Co-packaged diluents should follow the recommendations for drug products. A risk-based approach is recommended, where development data and excipient prior knowledge can be used to understand whether additional drug substance and/or drug product stability data are appropriate to support the re-test period or shelf life.

4 SELECTION OF BATCHES

4.1 Considerations for Selection of Primary Stability Batches

Where possible, batches of drug product included in stability testing should be derived from different batches of drug substance to account for variability in drug substance batches. Stability studies should be performed on each individual strength, fill volume and container closure system of the drug product unless a reduced protocol design is applied (refer to Annex 1 – Reduced Stability Protocol Design).

Table 2: Considerations for Primary Stability Batches of Drug Substance and Drug Product

	Synthetic Chemical Entities	Biologicals
Drug Substance	• Same chemical synthetic route • Similar manufacturing process (differences justified) • At minimum, all batches manufactured at pilot scale[2] • Meet proposed registration specification • Containers constructed of the same material and type of container closure system as production batches.	• Same cell production system, if applicable • Similar manufacturing process (differences justified) • Meet proposed registration release specification • Containers constructed of the same material and type of container closure system as production batches. • Comparable to production batches (ICH Q5E)
Drug Product	• Same formulation[1] and dosage form • Minimum of 2 batches manufactured to at least pilot scale[2], other batch(es) can be smaller if justified • Same manufacturing process with equipment with the same operating principles. • Meet the proposed registration release specification • Same fill unless a reduced protocol design is applied[1] • Same container closure system as proposed for marketing	• Same formulation and dosage form • Comparable to production batches (e.g., ICH Q5E) • Meet proposed registration release specification • Same fill volume unless a reduced protocol design is applied[1] • Same container closure system as proposed for marketing.

[1]Refer to Annex 1 – Reduced Stability Protocol Design for details around when exceptions may apply

[2]In accordance with ICH Q13, the definition of a pilot batch for synthetics does not apply for continuous manufacturing.

7 STORAGE CONDITIONS

4.1 Considerations for Selection of Primary Stability Batches

Table 3: Storage Condition Recommendations for Each Climatic Zone[1]

Climatic Zone[1]	Long-term[2]	Intermediate	Accelerated
I and II	25°C ± 2°C/60% RH ± 5% RH	30°C ± 2°C/65% RH ± 5% RH, or 30°C ± 2°C/75% RH ± 5% RH	40°C ± 2°C/75% RH ± 5% RH
	30°C ± 2°C/65% RH ± 5% RH, or 30°C ± 2°C/75% RH ± 5% RH	Not applicable	40°C ± 2°C/75% RH ± 5% RH
III	30°C ± 2°C/35% RH ± 5% RH, or 30°C ± 2°C/65% RH ± 5% RH, or 30°C ± 2°C/75% RH ± 5% RH	Not applicable	40°C ± 2°C/75% RH ± 5% RH
IVa	30°C ± 2°C/65% RH ± 5% RH, or 30°C ± 2°C/75% RH ± 5% RH	Not applicable	40°C ± 2°C/75% RH ± 5% RH
IVb	30°C ± 2°C/75% RH ± 5% RH	Not applicable	40°C ± 2°C/75% RH ± 5% RH

[1]Specific regional requirements for more severe storage conditions may however apply

[2]Refer to Section 1.3 – Introduction to Guideline and General Principles

8 PHOTOSTABILITY

The intrinsic photostability characteristics of a product should be evaluated to demonstrate that light exposure does not result in unacceptable change that could compromise product efficacy or patient safety. Normally, photostability testing is carried out on a single representative batch suitable for the purpose of the study. Repeating a photostability study may be required in response to relevant changes

Two specific studies are performed to generate and evaluate photostability data:

- Forced photodegradation study – A study that may be an integral part of forced degradation evaluation and may be undertaken in the development phase. This information may be used to evaluate the overall photosensitivity of the drug substance and drug product for method development purposes, degradation pathway elucidation and to inform control strategies (refer to Section 2-Development Stability Studies Under Stress and Forced Conditions).
- Confirmatory photostability studies – Studies performed when a risk of photodegradation has been identified. The purpose of the studies is to establish the photostability characteristics to understand the ability of the primary or secondary packaging material to protect light-sensitive products and the impact of light on product quality through manufacture, storage, transportation and in-use. These data may also support labelling (e.g., storage statements).

A systematic approach to photostability testing is recommended, covering as appropriate:

i) Tests on the drug substance and/or drug product directly exposed; and if necessary.

ii) Tests on the drug substance and/or drug product in the primary packaging; and if necessary.

iii) Tests on the drug substance and/or drug product in the secondary packaging.

8 PHOTOSTABILITY

The intrinsic photostability characteristics of a product should be evaluated to demonstrate that light exposure does not result in unacceptable change that could compromise product efficacy or patient safety. Normally, photostability testing is carried out on a single representative batch suitable for the purpose of the study. Repeating a photostability study may be required in response to relevant changes

Two specific studies are performed to generate and evaluate photostability data:

- Forced photodegradation study – A study that may be an integral part of forced degradation evaluation and may be undertaken in the development phase. This information may be used to evaluate the overall photosensitivity of the drug substance and drug product for method development purposes, degradation pathway elucidation and to inform control strategies (refer to Section 2-Development Stability Studies Under Stress and Forced Conditions).
- Confirmatory photostability studies – Studies performed when a risk of photodegradation has been identified. The purpose of the studies is to establish the photostability characteristics to understand the ability of the primary or secondary packaging material to protect light-sensitive products and the impact of light on product quality through manufacture, storage, transportation and in-use. These data may also support labelling (e.g., storage statements).

A systematic approach to photostability testing is recommended, covering as appropriate:

i) Tests on the drug substance and/or drug product directly exposed; and if necessary.

ii) Tests on the drug substance and/or drug product in the primary packaging; and if necessary.

iii) Tests on the drug substance and/or drug product in the secondary packaging.

8 PHOTOSTABILITY

Option 1:

For light exposure similar to the D65 (outdoor daylight) emission standard (as currently defined in, ISO/CIE 18909:2022) (17), an artificial daylight fluorescent lamp combining visible and ultraviolet (UV) outputs, xenon or metal halide lamp, including appropriate filter(s) is recommended as radiation light source.

Option 2:

A combined exposure to both cool white fluorescent and near ultraviolet lamp, which is capable of producing a light exposure similar to the ID65 (indoor daylight) emission standard, for which the ultraviolet lamp has at least 25% of the ultraviolet-A between 320 and 360 nm and at least 25% is between 360 and 400 nm.

Option 3:

Ambient/mild light conditions (predominantly light >400 nm during manufacturing, processing and in-use), for which a fluorescent or LED lamp is recommended.

9 STABILITY CONSIDERATIONS FOR PROCESSING AND HOLDING TIMES FOR INTERMEDIATES

9.1 General Considerations

Good manufacturing practices (GMP) and good distribution practices (GDP) require that controls are in place to ensure that intermediates (i.e., drug substance intermediates and drug product intermediates (including bulk drug products)) are manufactured and stored under appropriate conditions. Storage and/or transportation arrangements should not have deleterious effects on the subsequent processing, stability, safety, or quality of intermediates, in accordance with good distribution practices.

The data used to establish the holding time should cover the proposed holding times for the intermediates and the stability studies should be performed at relevant temperature and humidity conditions to support the expected storage conditions for the drug substance or drug product intermediate. If the temperature and humidity conditions used during these studies do not correspond with the storage conditions described in Section 7 - Storage Conditions of this guideline, other conditions should be justified.

Cumulative hold times are generally assessed as part of process validation. If a stability risk is identified, a cumulative holding time study may be necessary.

10 SHORT-TERM STORAGE CONDITIONS

The drug product labelling may specify a short-term storage condition for a drug product. Short term storage is a condition where the primary container closure is not breached and that is different form the long-term storage condition and the in-use period. The short-term storage condition does not need to be implemented by the patient/health care professional, as use of short-term storage is optional. The short-term storage condition is intended for convenience of the patient or health care professional in accordance with regional requirements based on anticipated storage of the drug product.

La progettazione di studi specifici sulla stabilità delle condizioni di conservazione a breve termine deve seguire i principi generali applicati agli studi di stabilità a lungo termine e deve considerare tutte le zone climatiche pertinenti. In genere, lo studio dovrebbe includere almeno 2 lotti. Il numero di lotti e le considerazioni relative al campione invecchiato devono basarsi sui principi generali descritti per gli studi di stabilità in uso.

11 IN-USE STABILITY

In-use conditions are defined as the conditions that mimic the intended use of the drug product after the primary container is first breached and, where applicable, through preparation, storage and administration as per the relevant instructions.

Products packaged in single-use containers for immediate use and not requiring preparation generally do not require an in-use period and would not be subject to in-use stability testing. Assembly of a combination of a drug product with a medical device for immediate use does not constitute preparation in the context of in-use stability testing.

The regulatory submission for these products should include in-use stability data, upon which the in-use period and instructions are based

The protocol should simulate the intended use of the product, as detailed in the relevant instructions (e.g., for a multi-dose product stored in a vial, the in-use studies should demonstrate that the container closure system can withstand the conditions of repeated insertion and withdrawal). When designing in-use studies, conditions under which a drug product could be used, including the maximum time the drug product will be exposed to different environmental factors during use, should be considered. For samples requiring preparation, including reconstitution, dilution, or co-mixing, the in-use studies should demonstrate the stability of the product through preparation and handling under the specified storage conditions for the maximum storage period.

11 IN-USE STABILITY

11.2.1 Selection of Batches

Generally, in-use stability data should be provided on two batches of representative drug product. Based on a risk assessment considering product knowledge and available primary stability data, alternative approaches to batch selection may be considered when appropriately justified. At least one of the batches should be chosen towards the end of its shelf life. If such results are not available, one batch should be tested at the final point of the submitted stability studies.

In-use stability data should be used to determine whether a declaration of an in-use period and storage condition are necessary. The in-use period and storage conditions should be stated on the labelling in accordance with regional regulations.
There may be scenarios where an established in-use period may not be needed in the labelling. For example, prepared orally administered products, stored in multi-dose containers with a defined supply that is intended for continuous use (not intermittent dosing), may not need to include an in-use period on the labelling if the demonstrated in-use stability data support storage for the intended use of the product.

12 REFERENCE MATERIALS, NOVEL EXCIPIENTS AND ADJUVANTS

This section covers stability considerations for reference materials, novel excipients (e.g., those used for the first time in a drug product or through a new route of administration) and adjuvants. Novel excipients and adjuvants are discussed due to their significant potential impact on the quality of the drug product.

Additives (e.g., stabilisers and preservatives) may degrade during the re-test period or shelf life of the drug substance or the shelf life of the drug product. These materials (additives) should be monitored during the stability program if there is an indication that their reaction, degradation, or depletion will adversely affect the quality of the drug product. Refer to Section 3.3 Stability-Indicating Critical Quality Attributes for general stability study design considerations.

13 DATA EVALUATION

A comprehensive stability data evaluation should take into consideration any stored intermediates, process hold times, any short-term storage outside of the long-term storage conditions, including the risk of excursions to the storage conditions and manipulations of the product to the completion of administration to the patient (in-use stability).

13.1.2 Start of Shelf Life for Synthetic Chemical Entity Drug Products

The start of shelf life should be the date of production, which is defined as the date of the first manufacturing step that combines drug substance with other ingredients.

In accordance with regional requirements, consider the following approaches:

- When the date of release is less than 30 days from the date of production, the start of shelf life of a drug product batch could instead be calculated from the date of release of that batch.
- For drug products consisting of a drug substance as a single ingredient, filled into the final drug product container, the initial date of the filling operation is taken as the date of production.

13.1.3 Start of Shelf Life for Biological Drug Products

The start of shelf life for biological drug products begin on the date of manufacture e.g., date of filtration and/or filling for a liquid drug product. When the drug product filling operation takes place over more than one day, then the initial date of the filling operation is taken as the date of manufacture. Other approaches used to define the start of shelf life can be used if justified.

13 DATA EVALUATION

There are many valid statistical methods to evaluate stability data to set a re-test period or shelf life from batches of substances, intermediates, or products. The statistical methodology used should be justified as suitable for the product type, the data set used for the analysis (batches, study design factors, etc.) and the purpose of the evaluation. The following sections outline selected, commonly used approaches and do not cover all situations (26, 27).

13.2.1 Linear Regression for an Individual Batch

13.2.2 Combining Batches

13.2.3 Scale Transformation of Data

13.2.4 Extrapolation and Stability Modelling

13.2.5 Extrapolation for Synthetic Chemical Entities

13.2.8 Extrapolation for Chemical Entities when Stored Frozen

13.2.9 Extrapolation for Biologicals

13 DATA EVALUATION

Approccio già presente in ICH Q1E

13.3 Data Evaluation for Multi-factor, Full-design Studies

13.3.1 Testing to Combine Batch Data per Individual Combination

If each factor combination is considered separately, the stability data can be statistically tested to combine those batch data for each individual combination. The shelf life for each non-batch factor combination can be estimated separately by applying the procedure described for single factor, full design

13.3.2 Testing to Combine Data for All Factors and Factor Combinations

If the stability data are tested to combine all factors and factor combinations and the results show that the data can be combined, a single shelf life across all combinations and longer than that estimated based on individual factor combinations may be proposed. The shelf life is longer because the width of the confidence limit(s) for the mean will become narrower as the amount of data increases when batches, strengths, container sizes and/or fills, etc. are combined into a single analysis of covariance (e.g., ANCOVA).

Approccio già presente in ICH Q1E

13 DATA EVALUATION

Annex 2 Stability Modelling

A2-1 Statistical Evaluation of Stability Data from Single or Multi-factor Study Designs

A2-1.1 Evaluation of Variability for Stability Data in Single-factor, Full Design Studies Using Linear Regression Models

A2-1.2 Linear Models to Assess Stability Profile Using Multiple Batches

A2-1.2-1 Fixed Effects Model

When only 3 batches are available representative of the production batches, the model may consider batch as a fixed effect rather than as a random variable, with a selected significance level (p-value) for intercept and slope of 0.25

Mixed Effects Model

A mixed effects model may be chosen when five or more batches are available for statistical evaluation so that batch can be treated as a random variable. A toleran interval-based approach using the linear mixed effects model may be applied to determine an extended shelf life beyond the period covered by long-term data.

13 DATA EVALUATION

Annex 2 Stability Modelling

A2-2 Enhanced Stability Modelling

When enhanced stability modelling is used, applicants are encouraged to consult with regulatory authorities to understand submission expectations. Focus is placed on the design and data evaluation of enhanced stability models that can evaluate and extrapolate linear and non-linear quality attribute changes over time and includes the use of prior knowledge.

A2-2.1 General Principles of Enhanced Stability Modelling

There are many types of stability models available or currently under development and, correspondingly, the tools to evaluate data from such stability models. This annex covers general principles of currently known kinetic, thermo-kinetic and mechanistic models as well as in silico or de novo computational methods that simulate known attribute stability profiles.

A2-2.2 Model Development

A2-2.2.1 Choice of Model Type

2.2.1 Selection of Critical Quality Attributes for Stability Modelling

A2-2.2.2 Selection of Data and Parameters to Construct a Stability Model

A2-2.3 Evaluation of Data for Stability Modelling

A2-2.4 Model Validation and Verification

A2-2.5 Risk Management and Model Lifecycle Considerations

14 LABELLING

14.1 Excursions Outside of a Labelling Claim

Transient temperature excursions outside of the label storage conditions, may be acceptable if justified and supported by stability data. An assessment of the risk and impact of handling, transport, and storage excursions outside the label claim at various stages throughout the overall supply chain requires a comprehensive knowledge of the supply chain and an understanding of a drug substance and drug product’s stability profile. Data from stability studies, including accelerated studies, stress testing or transport simulation studies (when appropriate) can be used to evaluate the effects of an excursion on the drug substance or drug product. Additionally, statistical evaluation or modelling can be leveraged to evaluate the impact of a storage condition excursion, provided sufficient knowledge of the degradation pathway is available and fits an appropriate model. Each excursion should be documented and handled within the corresponding quality management system or appropriate risk assessment.

15 STABILITY CONSIDERATIONS FOR COMMITMENTS AND PRODUCT LIFECYCLE MANAGEMENT

Lifecycle management in the context of stability includes initial stability testing and re-test period and shelf life determination, ongoing (annual) stability testing, and stability studies supporting approval changes or commitments over a product's lifecycle. This also includes the introduction of new dosage forms or new strengths/concentrations. Commitment stability studies include studies to confirm the initially proposed re-test period/shelf life for commercial manufacture

15.1 Commitment Stability Studies

Where the primary stability studies for a drug substance or drug product do not cover the proposed re-test period or shelf life period granted at the time of initial approval, a commitment should be made to continue the stability studies to confirm the proposed re-test period or shelf life.

15 STABILITY CONSIDERATIONS FOR COMMITMENTS AND PRODUCT LIFECYCLE MANAGEMENT

15.2 Ongoing Stability Studies

Ongoing stability studies are not required to align with the primary stability protocol; however, testing should continue through to the end of the re-test period or shelf life. As product knowledge is gained, the applicant may consider removal of testing of attributes not related to stability and/or reduce testing timepoints based on risk assessment as detailed in Section 3 - Stability Protocol Design. Reductions, including bracketing and/or matrixing approaches, based on stability knowledge and risk assessment should be justified in the regulatory submission, Any change in the reduced design post-approval should be evaluated for its impact to the product quality prior to modifying the annual stability protocol. While the testing intervals listed during product development may be appropriate in the pre-approval stage, reduced testing may be appropriate after approval where data are available that demonstrate adequate and consistent stability. Where data exist that indicate the stability of a product is not compromised, the applicant is encouraged to propose and justify, where applicable, a protocol which supports the reduction or elimination of specific testing (e.g., 9-month testing interval) or certain attributes (e.g., orthogonal testing) for post-approval, long-term studies

15 STABILITY CONSIDERATIONS FOR COMMITMENTS AND PRODUCT LIFECYCLE MANAGEMENT

15.3 Product Lifecycle Stability Studies

Product lifecycle stability studies are conducted under the accelerated, intermediate, or long-term storage conditions (as applicable) to support product lifecycle changes by assessing whether the change has an impact on any stability related quality attributes of the commercial drug substance or product under the labelled storage, handling and use conditions. A risk assessment should be conducted and can be used to justify the change and determine the need and extent of studies required to support changes after approval in compliance with regional requirements.

15 STABILITY CONSIDERATIONS FOR COMMITMENTS AND PRODUCT LIFECYCLE MANAGEMENT

15.4 Stability Studies to Support New Dosage Forms and New Strengths/Concentrations

A new dosage form or strength/concentration contains the same drug substance as included in the existing, approved drug product. Within scope of a new dosage form are new products with different administration route (e.g., oral to parenteral, intravenous to subcutaneous), new specific functionality/delivery systems (e.g., immediate release tablet to modified release tablet, lyophilised to liquid product) and different dosage forms of the same administration route (e.g., capsule to tablet, solution to suspension, vial to prefilled syringe).